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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/751,014	01/02/2004	Henk J. Franssen	MPS 4-87FD3	2390

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EXAMINER	
KALLIS, RUSSELL	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 05/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/751,014	FRANSSEN ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Sequence Rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth: Table 1 and Table 2 present polynucleotide sequences that do not have sequence identifiers. Further, the tables should be moved from the specification to the drawings and identified using a sequence identifier.

§ 1.821 Nucleotide and/or amino acid sequence disclosures in patent applications;

(d) Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Applicant must amend the claims, specification, and/or drawings to insert sequence identifiers.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4, 6-7 and 8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims tissue specific expression in the nodules of transformed soybean of a plant-expressible structural gene under the control of a recombinant DNA molecule comprising any Enod2 gene regulatory region that hybridizes under conditions of unspecified high stringency to the DNA sequence of Tables 1 and 2.

Applicant broadly claims expression of any plant expressible structural gene, other than an Enod2 structural gene, in the nodules of soybean by growing soybean transformed with a recombinant DNA construct comprising said plant expressible structural gene under regulatory control of DNA sequence that hybridizes under conditions of unspecified high stringency to the DNA sequences of Tables 1 and 2.

Applicant only describes Enod2 5' regulatory DNA sequences from SEQ ID NO: 1 from about nucleotide 520 to 1565 and from about nucleotide 1050 to 1565.

Applicant does not describe all other Enod2 regulatory DNA sequences that would bind to the DNA of Tables 1 and 2 and possess tissue specific Enod activity in nodules of soybean.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial

portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of Enod regulatory sequences. Applicants only describe 5' regulatory DNA sequences from SEQ ID NO: 1 from about nucleotide 520 to 1565 and from about nucleotide 1050 to 1565. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of Enod regulatory sequences that would be required for tissue specific activity. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for Enod tissue specific regulatory activity, it remains unclear what features identify an Enod tissue specific regulatory sequence. Since the genus of Enod regulatory sequences has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Sequences that hybridize with the DNA sequence in Tables 1 and 2 encompass naturally occurring allelic variants and mutants of Enod2 regulatory sequences, as well as sequences having no known Enod regulatory activity, of which Applicant is not in possession. Accordingly, the specification fails to provide an adequate written description to support the genus of Enod regulatory sequences encompassed by the hybridization language as set forth in the claims. (See Written Description guidelines published in Federal Register/Vol. 66, No.4/Friday, January 5, 2001/Notices: p.1099-1111).

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in

the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Applicant broadly claims expression of any plant expressible structural gene, other than an Enod2 structural gene, in the nodules of soybean by growing soybean transformed with a recombinant DNA construct comprising said plant expressible structural gene under regulatory control of DNA sequence that hybridizes under conditions of unspecified high stringency to the DNA sequences of Tables 1 and 2.

Applicant teaches isolation of a 1000bp Enod cDNA clone, Enod2, from 10 day old soybean nodule mRNA in a differential screen using cDNA probes made from mRNA isolated from 5 day old uninfected roots and mRNA isolated 10 days after inoculation (Example 1 pages 32-33), DNA sequencing of the Enod2 cDNA (Example 2 page 34), isolation of two genomic clones, Enod2a (SEQ ID NO: 1) and Enod2b (SEQ ID NO: 4), using the Enod cDNA as a probe (Example 3 pages 35-36), and identification of coding and both 3' and 5' non-coding regions of the Enod 2a and Enod2b genomic clones (Example 4 pages 36-37).

Applicant does not teach transformed and regenerated soybean expressing any heterologous plant expressible structural gene in developing soybean nodules under regulatory control of any 5' or 3' flanking sequences of either Enod2a or Enod2b genomic clones or any trans-acting non-Enod2 sequences, and any DNA sequences that hybridize under conditions of unspecified stringency to the DNA sequences of Table 1 and 2 (soybean Enod2a and Enod2b genomic clones).

The state of the art for soybean transformation and regeneration at the time of the claimed priority date of July 1, 1988 indicated in the declaration of the specification, was not enabling for the claimed invention. No published information of successful soybean transformation and regeneration had appeared until August 1988 (Widholm J. M., TibTech, November 1988, Vol. 6, pp. 265-266, column 1 lines 40-50, columns 2 and 3; McCabe *et al.* Bio/Technology Vol. 6, August 1998, pages 923-926 Abstract and columns 1 and 2; and Hinchee *et al.* Bio/Technology Vol. 6, August 1998, pages 915-921 column 2, lines 3-11 and 26-36).

Further, the unpredictability inherent in re-combining homologous regulatory gene sequences is exemplified in the loss of heritable activity of a target gene regulated by a promoter, the homologous copy of which, when inserted into a genome already containing the homologous endogenous copy of that promoter, and cannot be anticipated with any reasonable degree of predictability (Park Y. D. *et al.,* Plant Journal 1996, Feb. 9, (2): pp. 183-194, see Abstract).

The unpredictability inherent in re-combining homologous regulatory gene sequences is exemplified in the nature of DNA hybridization because it is permissive of non-homologous binding that is dependent upon the relative stringency of hybridization conditions, it is certain that gene regulatory DNA sequences that have only partial homology to an Enod regulatory

region or comprise only a partial complement of the regulatory DNA sequences of an Enod2 DNA regulatory region of claim 1, would be isolated under the undefined hybridization conditions of Claim 1. The unpredictability of recovering a predictable phenotype in a plant transformed with partial regulatory sequences or 5' regulatory sequences that are uncharacterized by a reduction to practice raises the issue of whether the entire portion required for tissue specific regulation has been isolated and is exemplified in the analysis of GUS gene expression in *Lotus* and soybean plants transformed with increasingly shortened lengths of a promoter for cytosolic soybean glutamine synthase. The results clearly show a loss of ammonium inducible promoter activity in roots and nodules when the length was shortened (Terce-Laforgue T. *et al.* Plant Mol. Bio. 1999, Vol. 39: pages 551-564; pp. 555 column 2, lines 35-46; page 556 column 1, lines 1-24; and figure 2).

Given the lack of guidance, the limited working examples in the specification, the breadth of the claims, and the unpredictability in the art, undue trail and error experimentation would have been required by one skilled in the art to isolate and regenerate into a plant a transformed soybean cell with the ability to express any type of plant expressible structural gene from a multitude of non-exemplified soybean transformation events or to evaluate a multitude of non-exemplified regenerated transgenic soybean plants transformed with myriad of non-exemplified plant expressible structural DNA under non-exemplified regulatory control of a multitude of flanking DNA from a gene expressed in developing soybean nodules seven days after planting or from other non-exemplified trans-acting genes that would hybridize to a Enod2 regulatory region.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Dependent claims are included in all rejections.

At Claim 1, line 4, "hybridizes" is indefinite. It is unclear because the conditions are unspecified and the specification does not set forth the metes and bounds of "high" stringency conditions.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a transformation step and a regeneration step.

Claim 4 is indefinite in that the claim is directed towards common regions of the Enod2a and Enod2b promoters yet it does not define or set forth those common sequences. Further it is not clear what are the metes and bounds of those portions common to Enod2a and Enod2b that display tissue specific regulatory activity.

Claims 1-8 are deemed free of the prior art, given the failure of the prior art to teach or suggest an isolated Enod2 regulatory region, or its ligation to a heterologous coding sequence, as stated in allowed parent application No. 08/411,062 now U.S. Patent 5,631,358.

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Russell Kallis Ph.D.
April 27, 2006

RUSSELL P. KALLIS, PH.D.
PRIMARY EXAMINER